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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,682	10/19/1999	DANUTA EWA IRENA MOSSAKOWSKA	88362/107	2932

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/380,682	Mossakowska
Examiner	**Art Unit**
Michael Brannock, Ph.D.	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Mar 28, 2002* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *Mar 4, 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);
   (b) ☐ they raise the issue of new matter. (See NOTE below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: _____
4. ☒ Applicant's reply has overcome the following rejection(s):
   See attachment
5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in separate, timely filed amendment cancelling the non-allowable claim(s).
6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
   See attachment
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
   Claim(s) allowed: _____
   Claim(s) objected to: _____
   Claim(s) rejected: *28-30, 42, 43, 49, and 50*
9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
11. ☐ Other:

Attachment to Advisory Action

1. Claims 28, 29 42, 43, 49 and 50 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the new reason below and for the reasons set forth in paragraphs b-d, and g of item 5 of Paper 14, reiterated and discussed below:

Applicant's proposed amendments of claims 28, 42, 49, and 50, to recite "of the SCR (SEQ ID NO: 59)" would render the claims indefinite for several reasons: "the SCR" lacks antecedent basis in the claim, i.e. which SCR is "the SCR"? The parenthetical reference to SEQ ID NO: 59 makes it unclear if SEQ ID NO: 59 is simply an example of "the SCR" and thus does not define the bounds of the term. SEQ ID NO: 59, as it appears in the sequence listing, is inconsistent with the definition of the term "SCR" as set forth in the specification at page 2, and in the prior art, wherein a SCR is defined as approximately 60 amino acids in length, whereas SEQ ID NO: 59 appears to comprise multiple SCRs.

b) The phrase "wherein at least one of the native amino acids is substituted" (e.g. claim 28) is indefinite because the claims do not set forth which polypeptide, nor which portion thereof, is considered "native", e.g. the sentence structure is ambiguous as to whether this phrase relates to SCR3 or to any other particular portion of the protein.

c) The positions of the proposed amino acid substitutions are indefinite (e.g. Val at position 4, claim 28) because the claim does not put forth where the numbering is to start from.

Applicant's purposed parenthetical reference to a sequence identifier does not stipulate that the numbering be in relation to SEQ ID NO: 59.

d) Claims 42, 43 and 49 require "derivatives" of the recited polypeptide. The word "derivatives" renders the claims indefinite because the claims include amino acid sequences and chemical modification not actually disclosed, thereby rendering the metes and bounds of the claim unascertainable. Applicant argues that derivatives are known in the art and defined in the specification. This argument has been fully considered but not deemed persuasive. The specification provides some examples of derivatives, however, examples are not sufficient to define the bounds of a claim. The specification does not provide guidelines for measuring the degree of "derivation" nor can the metes and bounds of the term "derivative" be ascertained when read in light of the specification. One of ordinary skill in the art, would not be reasonably apprised of the metes and bounds of the invention. The examiner cannot suggest an appropriate phrase, because the examiner does not understand the bounds of protection Applicant is seeking.

g) In claim 42 the term "thermodynamic additivity" renders the claim indefinite because there is no art-recognized definition of the term and nor is the description of the term at page 8 of the specification sufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not ""thermodynamic additivity". Applicant argues that this term has been well known to one skilled in the art and has been in practice. Applicant points to Murphy and Gill. et al. page 699, paragraph 1, lines 1-4, in support of this assertion. This

argument has been fully considered and discussed previously but not deemed persuasive; this term does not appear to be used by Murphy and Gill.

2. Claim 43 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polypeptide of SEQ ID NO: 1, yet the claim encompasses polypeptide derivatives not described in the specification, i.e. those comprising membrane binding sequences identified through screening of random chemical libraries. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the positions or identities of those sequences based on the information disclosed in the specification.

With the exception of the of the polypeptide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polypeptide of SEQ ID NO: 1, and polypeptides derivatives thereof comprising membrane binding elements taught in the specification, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant argues that the specification describes derivatives of membrane binding sequences in addition to SEQ ID NO: 1 at page 10 and 11 of the specification, as well as in the prior art. This argument has been fully considered but not deemed persuasive. There appears to be no description of any polypeptides comprising membrane binding sequences identified through screening of random chemical libraries, as is required by the claim.

3. Claims 28, 29, and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990, as set forth in item 9 of Paper 14, and reiterated below.

U.S. Patent No: 5545619 teaches a soluble polypeptide (CR1) comprising one to four short consensus repeats of the long homologous repeat A (LHR-A) and related polypeptides termed RCA polypeptides (see col 6), methods of producing mutations is said polypeptides (see col 7), and pharmaceutical compositions containing therapeutically effective amounts of same (see col. 9). By way of reference to Hourcade et al., U.S. Patent No: 5545619 discloses that amino acid sequences having the mutations recited in the instant claims are encompassed by the invention (see col. 6, lines 6-15). These mutations are disclosed by Hourcade et al., (see Figure 3), as pointed to by U.S. Patent No: 5545619. Claim 42 also requires that the polypeptide derivative comprises at least two heterologous membrane binding elements with low membrane affinity, covalently associated with the polypeptide, wherein the elements are capable of interacting independently and with thermodynamic additivity with the components of cellular

membranes exposed to extracelluar fluids. The instant specification states that preferred membrane binding elements are basic amino acid sequences (see the bottom of page 9). The amino acid sequence taught by Hourcade et al. provides for at least 8 heterologous basic amino acids (arginine and lysine) relative to CR1 (see Figure 3 of Hourcade et al.).

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, with reasonable expectation of success, to produce a polypeptide having the amino acid sequence taught by Hourcade et al. when practicing the invention disclosed in U.S. Patent No: 5545619. The motivation to do so was provided in U.S. Patent No: 5545619 wherein it was stated that the term "RCA proteins" refers to that taught by Hourcade et al. (see col. 6, lines 6-15), and that such proteins are useful in therapeutic and prophylactic contexts (see the last paragraph of col. 8).

Applicant's arguments regarding purposeful mutation versus allelic variation are unpersuasive. U.S. Patent No: 5545619 teaches that the mutations disclosed by Hourcade et al. (e.g. SCRs 1-7) are encompassed by the invention of U.S. Patent No: 5545619 (see col. 6, lines 6-15), and that hybrid proteins should be constructed wherein SCRs of one RCA protein can be combined with SCRs of one or more other RCA proteins (see col 6, lines 20-29). Thus, U.S. Patent No: 5545619 specifically contemplates purposeful substitution to arrive at the claimed polypeptides. Applicant argues that one would not have an expectation of success to make the claimed polypeptides because U.S. Patent No: 5545619 teaches that "it is unclear whether this CR1 gene sequence is expressed". This argument has been fully considered but not deemed

persuasive because U.S. Patent No: 5545619 clearly teach that these sequences are encompassed by the invention (see col. 6, lines 6-15).

4. Claims 43 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990, as applied to claims 28, 29, 42 and 50 above, and in further view of Clissold et al., Eur. J. Immunol., 23(2346-2352)1993 and U.S. Patent No: 5936092, as set forth previously in item 10 of Paper 14.

Applicants arguments are based on the applicability of U.S. Patent No: 5545619 in view of Hourcade et al.. These arguments have been fully considered and fully addressed above.

5. The rejection of claim 43 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No: 5936092, as set forth in 11 of Paper 18 would be withdrawn in view of Applicant's purposed amendments.

Conclusion

6. No claims are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

April 29, 2002

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600